APPLICATION STATEMENT

The application of the Clinical Coverage Guideline is subject to the benefit determinations set forth by the Centers for Medicare and Medicaid Services (CMS) National and Local Coverage Determinations and state-specific Medicaid mandates, if any.

DISCLAIMER

The Clinical Coverage Guideline (CCG) is intended to supplement certain standard WellCare benefit plans and aid in administering benefits. Federal and state law, contract language, etc. take precedence over the CCG (e.g., Centers for Medicare and Medicaid Services [CMS] National Coverage Determinations [NCDs], Local Coverage Determinations [LCDs] or other published documents). The terms of a member's particular Benefit Plan, Evidence of Coverage, Certificate of Coverage, etc., may differ significantly from this Coverage Position. For example, a member's benefit plan may contain specific exclusions related to the topic addressed in this CCG. Additionally, CCGs relate exclusively to the administration of health benefit plans and are NOT recommendations for treatment, nor should they be used as treatment guidelines. Providers are responsible for the treatment and recommendations provided to the member. The application of the CCG is subject to the benefit determinations set forth by the Centers for Medicare and Medicaid Services (CMS) National and Local Coverage Determinations, and any state-specific Medicaid mandates. Links are current at time of approval by the Medical Policy Committee (MPC) and are subject to change. Lines of business are also subject to change without notice and are noted on www.wellcare.com. Guidelines are also available on the site by selecting the Provider tab, then "Tools" and "Clinic Guidelines".

BACKGROUND

According to the American Cancer Society, nearly 213,000 new cases of breast cancer will be diagnosed in the United States in 2006 and almost 41,000 women will die of the disease. One factor that affects prognosis is whether or not the breast cancer has spread to the axillary lymph nodes. Over half of breast cancer patients have lymph node-negative (LN-) disease and are likely to remain free of tumor; however, disease recurs in about 30% of women with node-negative disease. Other prognostic factors such as tumor size, tumor grade, hormone receptor status, age, histology, and cell growth characteristics can define subgroups of women with LN- breast cancer who are at high risk for recurrence. However, these criteria have low accuracy for predicting disease progression and clinical outcome. Such uncertainty can result in inadequate treatment and disease recurrence for some patients and unnecessary treatment with a risk of serious side effects for others. Genetic profiling of tumors allows breast...
cancers to be classified based on their expression of specific genes that are related to the clinical behavior of the disease. Knowing if a patient's tumor expresses genes associated with disease recurrence can help in determining the appropriate treatment.¹

Oncotype DX™ is a diagnostic assay that quantifies the likelihood of breast cancer recurrence in women with newly diagnosed, early-stage, LN-, estrogen receptor positive (ER+) breast cancer. Data from the Oncotype DX assay are also used to estimate the potential benefit from chemotherapy. For this test, tumor tissue is excised surgically and sent to a pathology lab where it is fixed in formalin and embedded in paraffin. Micro sections are then cut from the paraffin block and placed in the provided Oncotype tubes. At Genomic Health, tissue RNA is extracted, purified, and analyzed for the expression of 21 genes using real-time RT-PCR (reverse-transcriptase polymerase chain reaction). The results are provided as a Recurrence Score™ (RS) that ranges from 0 to 100. Patients are grouped into low-, intermediate- and high-risk categories with higher scores corresponding to higher risk. The physician can use this information along with other data to make treatment decisions.²

The National Comprehensive Cancer Network (NCCN) (2008) discusses the use of gene expression profiling in the management of breast cancer patients and proposes that this technology will play an important role as a prognostic tool in the future. NCCN states “While many of the DNA microarray technologies are able to stratify patients into prognostic and/or predictive subsets on retrospective analysis, the gene subsets appear to differ from study to study, and prospective clinical trials testing the utility of these techniques have yet to be reported.” Pending the results of the TAILORx and MINDACT clinical trials, the NCCN Panel considers Oncotype DX as an option for evaluating “primary tumors characterized as 0.6–1.0 cm with unfavorable features or >1 cm and node-negative, hormone-receptor positive and HER2-negative.” In this circumstance, the recurrence score may assist in estimating the likelihood of recurrence and benefit from chemotherapy.” They stress that the recurrence score should be used “for decision making only in the context of other elements of risk stratification.”³

### Staging ³

**Breast cancer staging** is used to determine the extent of the disease upon diagnosis. The stage of the disease is important to develop an appropriate treatment plan and determine the prognosis (expected outcome of the disease). Physical examination, imaging tests (e.g., mammogram, ultrasound), and pathology results following biopsy or other surgery are used to stage breast cancer. The tumor, node, metastasis (TNM) system classifies cancer by tumor size (T), the degree of regional spread or lymph node involvement (N), and distant metastasis (M). Using this system, breast cancer is assigned a stage from I to IV.

**Stage 0** breast cancer sometimes is considered a pre-cancerous condition. Ductal carcinoma in situ (DCIS) is an example of stage 0 breast cancer. In DCIS, cancer cells are located within a milk duct, but have not invaded breast tissue or spread to lymph nodes or distant sites. Other types of breast cancer that may be classified as stage 0 include lobular carcinoma in situ (LCIS) and Paget disease of the nipple.

In **Stage I** breast cancer, the tumor is 2 cm or less in diameter (T1) and cancer cells have not spread to lymph nodes (N0) or to distant sites (M0).

**Stage II** breast cancer is classified as stage IIA or stage IIB. A stage IIA classification involves the following:
- No tumor is located in the breast (T0), but cancer cells are found in 1–3 axillary (under the arm) lymph nodes (N1) and have not spread to distant sites (M0); or
- Tumor is less than 2 cm in diameter (T1) and cancer cells have spread to 1–3 axillary lymph nodes (N1), but not to distant sites (M0); or
- Tumor is larger than 2 cm and less than 5 cm in diameter (T2) and cancer cells have not spread to axillary nodes (N0) or to distant sites (M0).

**Stage IIB** classification of breast cancer involves the following:
- Tumor is larger than 2 cm and less than 5 cm in diameter (T2) and cancer cells have spread to 1–3 axillary lymph nodes (N1), but not to distant sites (M0); or
- Tumor is larger than 5 cm and does not grow into the chest wall (T3) and cancer cells have not spread to lymph nodes (N0) or to distant sites (M0).
Breast cancer also is classified as stage IIB when sentinel node biopsy, but not imaging tests or clinical examination, shows that cancer cells have spread to internal mammary lymph nodes. Classifications for stage III breast cancer include stage IIIA, stage IIIB, and stage IIIC. Stage IIIA involves the following:

- Tumor is less than 5 cm in diameter (T0–T2) and cancer cells have spread to 4 to 9 axillary lymph nodes (N2), but not to distant sites (M0); or
- Tumor is larger than 5 cm (T3) and cancer cells have spread to 1 to 9 axillary nodes (N0–N2) or to internal mammary nodes, but not to distant sites (M0).

In stage IIIB breast cancer, the tumor has grown into the chest wall or the skin (T4) and cancer cells may have spread to as many as 9 axillary nodes (N0–N2), but not to distant sites (M0).

Stage IIIC breast cancer involves a tumor of any size (T0–T4) and cancer cells that have spread to 10 or more axillary lymph nodes, or to 1 or more other regional lymph nodes, or to internal mammary lymph nodes (enlarging these nodes) on the same side as the tumor (N3), but not to distant sites (M0). Inflammatory breast cancer also is classified as stage III, unless it has spread to a distant site.

Stage IV breast cancer is a tumor of any size (T0–T4) and cancer cells that may have spread to nearby lymph nodes (N0–N3) and have spread to a distant site (M1). Common sites of metastasis include the bones, liver, lungs, brain, and distant lymph nodes.

American Society of Clinical Oncology (ASCO) The ASCO published an update in 2007 to the recommendations of the use of tumor markers in the treatment and management of breast cancer. This guideline indicates that, in newly diagnosed patients with N–, ER+ breast cancer, the Oncotype DX assay can be used to predict the risk of recurrence in patients treated with tamoxifen. The Oncotype DX assay may be used to identify those patients who will obtain the most benefit from adjuvant tamoxifen and may not require adjuvant chemotherapy. Furthermore, patients with a high RS may respond better to adjuvant chemotherapy than from tamoxifen. However, there were insufficient data at the time to know if these recommendations could be extended to other hormone therapies besides tamoxifen or other chemotherapy regimens.

**POSITION STATEMENT**

**Applicable To:**
- Medicaid – Hawaii
- Medicare – Hawaii, Easy Choice Health Plan (California)

**NOTE:** For all other lines of business, please refer to the current contracted vendor for Lab Management requests.

The genetic assay Oncotype DX™ is considered medically necessary to assess the need for adjuvant chemotherapy in women with recently diagnosed breast cancer when ALL of the following criteria are met:

- Breast tumor is stage 1 or stage 2; AND,
- Breast tumor is Estrogen-Receptor Positive; AND,
- Breast tumor is HER2-receptor negative; AND,
- There is no evidence of metastatic breast cancer, and the member is axillary-node negative; AND,
- The member is a candidate for possible adjuvant chemotherapy (i.e., chemotherapy is not precluded due to other factors), and testing is being done specifically to guide the decision as to whether or not adjuvant chemotherapy will be used.

Oncotype DX™ is considered experimental and investigational and NOT a covered benefit for any other clinical evaluation.

All other assays of genetic expression in tumor tissue (e.g., Breast Cancer Gene Expression Ratio, MammaPrint®, Rotterdam Signature 76-Panel) are considered experimental, investigational and clinically unproven.

Oncotype DX® is considered experimental and investigational and NOT a covered benefit for patients with ductal carcinoma in situ (DCIS). According to Hayes (2012) a lack of published evidence exists for use of DCIS; data were insufficient for analytical validity, clinical validity, and clinical utility.
GENETIC ASSAY FOR BREAST CANCER (ONCOTYPE DX™)
HS-079

CODING

CPT® Code - Covered when ALL of the above criteria are met.
81479  Unlisted molecular pathology procedure (claims prior to 01/04/2015)
81519  Oncology (breast), mRNA, gene expression profiling by real-time RT-PCR of 21 genes, utilizing formalin-fixed paraffin embedded tissue, algorithm reported as recurrence score (claims received on and after 01/01/2015)

HCPCS Level II Code
S3854* Gene expression profiling panel for use in the management of breast cancer treatment
*S- Codes are NON COVERED FOR MEDICARE – Refer to HCPCS Level II Temporary National Codes

ICD-10-CM Diagnosis Codes - Covered when ALL of the above criteria are met.
C50.011 - C50.029  Malignant neoplasm of nipple and areola, female, male
C50.111 - C50.129  Malignant neoplasm of central portion of breast, female, male
C50.211 - C50.229  Malignant neoplasm of upper-inner quadrant of breast, female, male
C50.311 - C50.329  Malignant neoplasm of lower-inner quadrant of breast, female, male
C50.411 - C50.429  Malignant neoplasm of upper-quadrant of breast, female, male
C50.511 - C50.529  Malignant neoplasm of lower-quadrant of breast, female, male
C50.611 - C50.629  Malignant neoplasm of axillary tail of breast, female, male
C50.811 - C50.829  Malignant neoplasm of overlapping sites of breast, female, male
C50.911 - C50.929  Malignant neoplasm of breast of unspecified site, female, male
D05.00 – D05.92  Carcinoma in situ of breast
Z17.0  Estrogen receptor positive status [ER+]

Non-Covered ICD-10-CM Diagnosis Code
D05.10- D05.12  Intraductal carcinoma in situ of breast

Coding information is provided for informational purposes only. The inclusion or omission of a CPT, HCPCS, or ICD-10 code does not imply member coverage or provider reimbursement. Consult the member’s benefits that are in place at time of service to determine coverage (or non-coverage) as well as applicable federal / state laws.

REFERENCES


MEDICAL POLICY COMMITTEE HISTORY AND REVISIONS

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<td>11/2/2017, 12/8/2016</td>
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<tr>
<td>11/5/2015</td>
<td>Approved by MPC. Updated coding.</td>
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<tr>
<td>8/7/2014</td>
<td>Approved by MPC. Updated lines of business.</td>
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<td>6/5/2014</td>
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<td>2/7/2013</td>
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<td>4/5/2012</td>
<td>Approved by MPC. Addition of Hayes 2012 recommendation on DCIS.</td>
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<tr>
<td>2/2/2012</td>
<td>Approved by MPC. New reference reflecting ASCO recommendations.</td>
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